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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/401,636	09/22/1999	LARS T. HELLMAN	10223/006001	4922

26191 7590 10/05/2004

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EXAMINER

HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 10/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/401,636

Applicant(s)

HELLMAN, LARS T.

Examiner

Phuong Huynh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE Three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 55-83 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 83 is/are allowed.
- 6) ☒ Claim(s) 55-61, 64-68 and 70-82 is/are rejected.
- 7) ☒ Claim(s) 62, 63 and 69 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3/29/04; 7/19/04.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

1. Claims 55-83 are pending.
2. The following new grounds of rejections are necessitated by the amendment filed 7/19/04.
3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
4. Claims 55-61, 64-68, and 70-82 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) an immunogenic polypeptide comprising a human IgE CH3 domain located between two non-placental mammalian IgE domains wherein said one of said two non-placental mammalian IgE domains is an opossum IgE CH2 domain and the other of said two non-placental mammalian IgE domains is an opossum IgE CH4 domain and wherein said immunogenic polypeptide is effective to induce an anti-human IgE response in human, (2) an immunogenic polypeptide comprising a human IgE CH3 domain located between two non-placental mammalian IgE domains wherein the sequence of said immunogenic polypeptide is as set forth in SEQ ID NO: 8, (3) an immunogenic polypeptide comprising two human IgE CH3 domain located between three non-placental mammalian IgE domains wherein said first of said three nonplacental mammalian IGE domains is an opossum IgE CH2 domain, wherein said second of said three non-placental mammalian IgE domains is an opossum IgE CH2 domain and wherein said third of said three non-placental mammalian IgE domains is an opossum IgE CH4 domain, (4) an immunogenic polypeptide comprising four human IgE CH3 domains and three non-placental mammalian IgE domains wherein said first of said three non-placental mammalian IgE domains is an opossum IgE CH2 domain, wherein said second of said three non-placental mammalian IgE domains is an opossum IgE CH2 domain and wherein said third of said three non-placental mammalian IgE domains is an opossum IgE CH4 domain and (4) an immunogenic polypeptide as set forth in claim 83, **does not** reasonably provide enablement for *all* immunogenic polypeptide as set forth in claims 25-26, 28-34, and 36-40 for inducing any anti-self IgE response in a human. The specification does not enable any person skilled in the art to

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which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only immunogenic polypeptides such as the ones shown in Fig 2. The specification discloses immunogenic polypeptide comprising a human IgE CH3 domain located between opossum CH2 and opossum CH4 domain. An immunogenic polypeptide as set forth in SEQ ID NO: 8. An immunogenic polypeptide comprising two human IgE CH3 domains located between three non-placental mammalian IgE domains wherein said first of said three non-placental mammalian IgE domains is an opossum IgE CH2 domain, wherein said second of said three non-placental mammalian IgE domains is an opossum IgE CH2 domain and wherein said third of said three non-placental mammalian IgE domains is an opossum IgE CH4 domain. The specification further discloses an immunogenic polypeptide comprising four human IgE CH3 domains and three non-placental mammalian IgE domains wherein said first of said three non-placental mammalian IgE domains is an opossum IgE CH2 domain, wherein said second of said three non-placental mammalian IgE domains is an opossum IgE CH2 domain and wherein said third of said three non-placental mammalian IgE domains is an opossum IgE CH4 domain and an immunogenic polypeptide as set forth in claim 83. The immunogenic polypeptide mentioned above further comprises a polyhistidine sequence and wherein said immunogenic polypeptide is capable of dimerizing.

The specification does not teach how to make all immunogenic polypeptides as set forth in claims 55-61, 64-68, and 70-82 mentioned above because there is insufficient guidance as to which two, or three of which non-placental mammalian IgE domains in the claimed immunogenic polypeptide that would stabilize a functional conformation of human IgE such that anti-human IgE response is induced. There is insufficient guidance as to the ordering of the IgE domains in the claimed immunogenic polypeptide.

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Nechansky *et al* teach that “although it was shown that Cε3 is the region exclusively involved in the interaction with FcεRI, the synthesis of a recombinant single Cε3 domain still being able to bind to FcεRI with high affinity has never been successful” (See page 296, col. 1, first paragraph, in particular).

Further, there are more than 270 living species of non-placental mammals. There is insufficient guidance as to the structure of IgE sequence of all non-placental mammals, much less about the specific IgE domains. Even if the two or three non-placental IgE domains are limited to the non-placental mammal such as the ones recited in claims 56 and 73, the IgE sequence of koala, kangaroo, wallaby and wombat have not even been cloned, let alone which two or three CH2 and CH4 domains from koala, kangaroo, wallaby and wombat connected to human CH3 domain would form an immunogenic polypeptide that is effective to induce anti-human IgE response in a human. Further, the term “has” in claim 56 is open-ended. It expands the non-placental mammalian IgE domains to include additional amino acids at either or both ends, in addition to the problem mentioned above. There is a lack of guidance as to which amino acids to be added and whether the resulting sequence maintains its structure and effective to induce an anti-human IgE response.

Stryer *et al* teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo *et al*., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Kuby *et al*, of record, teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide.

Abaza *et al*, of record, teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with antibody against the site (See abstract, in particular). Without the amino acid sequence, it is unpredictable which

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undisclosed immunogenic polypeptide would be useful as a vaccine for inducing anti-human IgE response in a human.

With regard to claim 72, there is insufficient guidance as to the structure of the "at least N-terminal half of a human IgE CH3 domain" in the claimed immunogenic polypeptide without the amino acid sequence. Given the indefinite number of immunogenic polypeptide, there are insufficient in vivo working examples demonstrating that all undisclosed immunogenic polypeptide is effective for inducing an anti-human IgE response in a human. Since the immunogenic polypeptide is not adequately described, it follows that said immunogenic polypeptide comprises a polyhistidine sequence that is capable of dimerizing is not adequately described. Until the two or three domains of IgE from non-placental mammal such as koala, kangaroo, wallaby and wombat have been cloned; it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of *Ex parte Aggarwal*, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). In *re wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

5. Claims 55-61, 64-68, and 70-82 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of *all* immunogenic polypeptide as set forth in claims 55-61, 64-68, and 70-82 for inducing any anti-self IgE response in any mammal.

The specification discloses only immunogenic polypeptides such as the ones shown in Fig 2. The specification discloses immunogenic polypeptide comprising a human IgE CH3 domain located between opossum CH2 and opossum CH4 domain. An immunogenic polypeptide as set forth in SEQ ID NO: 8. An immunogenic polypeptide comprising two human IgE CH3 domains located between three non-placental mammalian IgE domains wherein said first of said three nonplacental mammalian IGE domains is an opossum IgE CH2 domain, wherein said

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second of said three non-placental mammalian IgE domains is an opossum IgE CH2 domain and wherein said third of said three non-placental mammalian IgE domains is an opossum IgE CH4 domain. The specification further discloses an immunogenic polypeptide comprising four human IgE CH3 domains and three non-placental mammalian IgE domains wherein said first of said three non-placental mammalian IgE domains is an opossum IgE CH2 domain, wherein said second of said three non-placental mammalian IgE domains is an opossum IgE CH2 domain and wherein said third of said three non-placental mammalian IgE domains is an opossum IgE CH4 domain and an immunogenic polypeptide as set forth in claim 83. The immunogenic polypeptide mentioned above further comprises a polyhistidine sequence and wherein said immunogenic polypeptide is capable of dimerizing.

With the exception of the specific immunogenic polypeptide mentioned above, there is insufficient written description about the structure as to which two or three “non-placental mammalian IgE domains” are part of the claimed immunogenic polypeptide (claims 55, 57, 58, 64, 65, 67, 68, 72, 74, 75 and 82).

There are more than 270 living species of non-placental mammals. There is insufficient guidance as to the structure of IgE sequence from all non-placental mammals, much less about the specific IgE domains in the claimed immunogenic polypeptide. Even if the two or three non-placental IgE domains are limited to the non-placental mammal such as the ones recited in claims 56 and 73, the IgE sequence of koala, kangaroo, wallaby and wombat have not even been cloned. Therefore all immunogenic polypeptide comprising a human IgE CH3 domain located between any two or three non-placental mammalian IgE domains from koala, Kangaroo, wallaby and wombat are not adequately described. Further, the term “has” in claim 56 is open-ended. It expands the non-placental mammalian IgE domains to include additional amino acids at either or both ends, in addition to the problem mentioned above. There is inadequate written description about which amino acids to be added and whether the resulting sequence maintains its structure and effective to induce an anti-human IgE response.

With regard to claim 72, there is inadequate written description about the structure of the “at least N-terminal half of a human IgE CH3 domain” in the claimed immunogenic polypeptide without the amino acid sequence.

Since the immunogenic polypeptide is not adequately described, it follows that said immunogenic polypeptide comprises a polyhistidine sequence that is capable of dimerizing is not adequately described.

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Finally, the specification discloses only three IgE sequences from non-placental mammal such opossum, platypus and wombat, and given the divergent of IgE sequence of platypus from said other non-placental mammals, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co.* 43 USPQ2d 1398; *University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 (CA FC2004).

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.
7. Claims 64-69 and 82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "...**two** human IgE CH3 domains and **three** non-placental..." in claim 64 has no antecedent basis in base claim 55 because claim 55 recites "An immunogenic polypeptide comprising **a** human IgE CH3 domain located between **two** non-placental mammalian IgE...

The "...**four** human IgE CH3 domains and **three** non-placental mammalian IgE domains" in claim 67 has no antecedent basis in base claim 55 because claim 55 recites "An immunogenic polypeptide comprising **a** human IgE CH3 domain located between **two** non-placental mammalian IgE...

An immunogenic polypeptideconnected to a non-placental mammalian means" in claim 82 is indefinite and ambiguous because it is not clear what is meant by "non-placental mammalian means". Is it a polypeptide or polynucleotide from non-placental mammalian connected to human IgE CH3 polypeptide as a means for inducing an anti-human IgE response in a human?

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8. Claims 62-63, and 69 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. Claim 83 is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

12. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

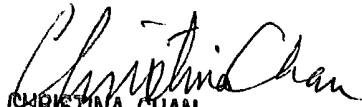
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Phuong N. Huynh, Ph.D.

Patent Examiner

Technology Center 1600

September 30, 2004


CHRISTINA CHAN
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